

REMARKS/ARGUMENTS

I. Amendments to the Specification:

The specification has been amended to correct minor clerical errors in the application. No new matter has been added by way of the instant amendments to the specification.

II. Amendments to the Claims:

Claims 1-77 were pending in the instant application. In response to the Restriction Requirement mailed April 3, 2006, Applicants elected claims of Group III, claims 44-69 for examination on the merits. Accordingly, the Examiner withdrew claims 1-43 and 70-77 from consideration as being drawn to non-elected subject matter.

Claims 1-43 and 70-77 are canceled herein without prejudice or disclaimer of the subject matter contained therein. Applicants reserve the right to pursue the subject matter of these claims in this or a future related application.

Claims 44-69 are currently pending and under examination in this application. Claims 47, 49, 51, and 53 are amended herein. Support for the amendments can be found throughout the specification as filed, including the original claims. Accordingly, no new matter has been added by way of the amendments to the claims.

Applicants acknowledge that the Examiner has indicated that claims 48 and 50-56 are free of the prior art (*see*, Office Action, page 10).

III. Information Disclosure Statement:

The Office Action indicated that several references in the Information Disclosure Statement filed February 20, 2004, were not considered because they failed to comply with the provisions of 37 C.F.R. §§ 1.97 and 1.98, and MPEP 609 (*see*, Office Action, page 2).

Applicants submit herewith a Supplemental Information Disclosure Statement (*see*, **Appendix A**) that Applicants aver is in full compliance with the provisions of 37 C.F.R. §§ 1.97 and 1.98, and MPEP 609. Applicants respectfully request that the Examiner consider the cited references and initial and return the Form-1449 with the next office communication.

IV. Claim Objection:

Claim 47 was objected to for reciting the limitation "R6" instead of "R₆" (*see*, Office Action, page 3).

In the instant Amendment and Response, claim 47 has been amended to correct the typographical error noted above.

Accordingly, Applicants respectfully request that this objection be reconsidered and withdrawn.

V. Rejections Under 35 U.S.C. § 112, First Paragraph, Written Description:

Claims 44-47, 49, 57-60, and 62 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement (*see*, Office Action, pages 3-4).

Without acquiescing to this rejection and solely to expedite prosecution, Applicants have canceled claims 44-46, 50, and 57-59. With respect to the rejection relating to the recitation of "hydrophobic amine" in claims 47, 49, 60, and 62, Applicants draw the Examiner's attention to currently amended claims 47, 49, 60, and 62, which recite, in relevant part, "a hydrophobic amine selected from the group consisting of a phenothiazine and a tricyclic antidepressant."

Applicants aver that this amendment puts claims 47 and 60, and the claims depending therefrom (*i.e.*, claims 48, 49, 51-56, 61, 62, and 64-69) in full compliance with the written description requirement.

Therefore, Applicants respectfully request reconsideration of this rejection and withdrawal of the same.

VI. Rejections Under 35 U.S.C. § 112, First Paragraph, Enablement:

Claims 57-69 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement (*see*, Office Action, pages 5-9). Specifically, the Office Action alleges that:

(i) although the relative skill of those in the art is high, that fact is outweighed by the purported unpredictability of the art as evidenced by Virador *et al.* (*Anal. Biochem.* **270**:207-219, 1999) and Seiberg *et al.* (*J. Invest. Dermatol.* **115**:162-67; 2000);

(ii) the claims are broad in claiming a general method of reducing skin pigmentation without limitation to a particular condition;

(iii) the specification provides no direction or guidance for determining particular administration regimes (dosages, timing, administration routes, etc.) necessary to reduce skin pigmentation in humans, and have limited working examples; and

(iv) an ordinary skilled artisan would have to carry out additional experiments to practice the claimed invention (*see*, Office Action, pages 5-9).

Applicants respectfully traverse this rejection for the following reasons.

With respect to point (i), the Office Action relies on Virador and Seiberg to purport that the art of modulating melanogenesis is unpredictable. The Office Action notes that Virador teaches that “there has been a great variation in studies on various bioactive compounds targeted at regulating melanin production.” However, Applicants respectfully aver that this teaching must be read in context of the *entire* sentence at page 207, right column, and in context of the *full* article. Virador is directed to providing a standardized protocol for assaying compounds that can be used for modulating pigmentation. This reference does not in any way teach or suggest that art of modulating melanogenesis in humans is unpredictable. In fact, this reference relies on numerous compounds that were known to modulate pigmentation including, kojic acid, hydroxyquinone, arbutin, niacinamide, MSH and thymidine dimers, which evidence the fact that such compounds for modulating melanogenesis were known in the art at the time of the instant application. Certainly, the availability of numerous pigmentation modulators is evidence of predictability in this art. This position is further supported by Seiberg, which teaches that serine protease inhibitors may be used as alternatives for depigmentation. The Office Action states that Seiberg teaches that hyperpigmentation disorders are often treated with hydroxyquinones, retinoids, and tyrosinase inhibitors, but that the results from such treatments are sometimes disappointing. This teaching simply suggests

that some of these treatments do not always work to the extent expected. This is far different from a demonstration that modulating melanogenesis in humans is unpredictable.

With respect to point (ii), Applicants note that the levels of melanin produced by melanocytes determine skin pigmentation. This fact is unaffected by the type of skin condition involved. In the instant application, Applicants have shown that compounds that mislocalize tyrosinase, and/or inhibit late endosomal/lysosomal trafficking in melanocytes, inhibit melanin production in melanocytes, thereby reducing skin pigmentation. Thus, compounds that are capable of either or both of these properties can reduce skin pigmentation regardless of the skin condition. Accordingly, Applicants respectfully aver that they are entitled to the full scope of their claim without limitation to any particular skin condition.

With respect to point (iii), Applicants respectfully disagree with the Office Action's position that adequate guidance for administrative regimes (*i.e.*, dosages, timing, administration, etc.) for reducing skin pigmentation have not been provided in the application as filed. With respect to guidance relating to "dosages and timing," Applicants draw the Examiner's attention to page 60, line 20 to page 61, line 18 of the application as filed. With respect to guidance relating to "methods of administration," Applicants draw the Examiner's attention to page 61, line 20, to page 70, line 23 of the application as filed. Thus, in view of this disclosure, Applicants respectfully aver that Applicants have provided sufficient guidance to the ordinarily skilled artisan for administrative regimes for reducing skin pigmentation.

The Office Action also opines that because the working examples are limited to *in vitro* assays of melanin production, they provide no guidance to the ordinarily skilled artisan to (a) formulate a composition for application to skin, and (b) determine whether a particular compound reduces skin pigmentation. Applicants respectfully disagree. With respect to formulating compositions for application to skin, Applicants again draw the Examiner's attention to the disclosure at page 61, line 20, to page 70, line 23 of the application as filed. Regarding determination of whether a particular compound reduces skin pigmentation, Applicants note that the experiments described in Example 6, at pages 78-79 of the application as filed, provide adequate guidance. The melan-a melanocyte model is a well-accepted model

system to study skin pigmentation as evidenced by the Virador reference cited by the Examiner (*see*, pages 210-211). Applicants note that the Federal Circuit has not construed the enablement requirement to require that Applicants provide actual evidence of success in treating humans. Instead, the courts have repeatedly held that all that is required is a reasonable correlation between the activity and the asserted use. *See, Nelson v. Bowler*, 626 F.2d 853, 857 (CCPA 1980). A rigorous or an invariable exact correlation is not required. *Cross v. Iizuka*, 753 F.2d 1040 (Fed. Cir. 1985). In the instant case, the pigmentation studies using melan-a melanocytes in Example 6, provide an example of such a reasonable correlation.

Finally, with respect to point (iv), Applicants first note, as argued in response to point (i) above, that the instant claims are not in an unpredictable art. As the Examiner has stipulated, the level of skill in the art is high. Accordingly, there is sufficient guidance provided in the instant specification for the "ordinary" skilled artisan to practice the claimed invention. Even if the ordinary skilled artisan would need to do additional experiments, such additional experimentation would not be undue. Applicants note that the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). In the instant case, at the time the application was filed, numerous skin pigmentation-modifying compounds were known as were assays to test their efficacy *in vivo*. Thus, in the context of the instant invention, an artisan who finds a compound recited in claim 60 to be effective *in vitro* can readily confirm that it will also work in an animal or other model. Such experimentation is not undue as the art typically engages in such experimentation.

In view of the foregoing remarks, Applicants respectfully aver that this rejection be reconsidered and withdrawn.

VII. Rejections Under 35 U.S.C. § 112, Second Paragraph:

Claims 44-56 were rejected under 35 U.S.C. § 112, second paragraph, for purportedly being indefinite, because of the limitation “results in a decrease in melanin product,” recited in claim 44 (*see*, Office Action, page 10).

Claim 44 has been canceled. Accordingly the grounds for this rejection have been rendered moot. Applicants further note that currently amended claim 47, recites in relevant part, “results in a decrease in melanin production.” This phrase is both definite and has antecedent basis because the preamble of this claim recites, “A method of decreasing melanin production . . .”

In view of the foregoing remarks, Applicants respectfully request that this rejection be reconsidered and withdrawn.

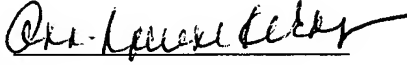
CONCLUSION

No fees are due in connection with this correspondence. However, if any fees are due, please charge the requisite fee or credit any overpayments to our Deposit Account No. 08-0219.

The Examiner is encouraged to telephone the undersigned at the number listed below in order to expedite the prosecution of this application.

Respectfully submitted,

Dated: October 6, 2006


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APPENDIX A

Attached are a Supplemental Information Disclosure Statement, Form-1449, and the cited references.